REMARKS

Claims 2-6, and 10 have been amended herein. Claims 15-17 are newly added. Claims 12 and 13 currently stand withdrawn pursuant to the earlier restriction requirement. Claims 1-11 and 14-17 remain active.

Claims 2 and 3 have been amended to address the §112, second paragraph issue noted in the Office Action (see the immediately following section of this response).

Claims 4, 5, and 6 have been amended to be independent claims that incorporate all of the subject matter of their respective base claims and any intervening claims.

Claim 10 has been amended to be an independent claim and further amended to include the subject matter of Claim 4 (*i.e.*, the capping groups X and Y are now explicitly recited in Claim 10).

New Claim 15 depends from Claim 5 and explicitly recites the capping groups X and Y from Claim 4. New Claim 16 depends from Claim 6 and also explicitly recites the capping groups from Claim 4. New Claim 17 recites the R^1 and R^2 groups from Claim 11, as well as the capping groups X and Y from Claim 4.

The term "capping group" has been replaced throughout the claims with the phrase "protecting group." Explicit support is found at page 4, last paragraph of the specification as filed.

All of the amendments to the claims enjoy verbatim support from the claims as originally filed. No new matter is added. Favorable reconsideration is respectfully requested.

Rejection of Claims 2 and 3 Under §112, Second Paragraph:

This rejection is believed to have been overcome by appropriate amendment to the claims. Specifically, Claims 2 and 3 have been amended to note that the chemical structure shown is one of the possibilities for the "A" substituent as shown in Claim 1. Each of Claims 2 and 3 have also been amended to positively recite that the variables X, Y, R^1, R^2 and n, "are as defined in Claim 1."

Applicants thus submit that this rejection has now been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1-3, 5-11, and 14 under §112, First Paragraph (Written Description):

This rejection have been overcome, in part, by appropriate amendment to the claims. The claims have been amended throughout to replace the phrase "capping group" with the phrase "protecting group." An extensive list of protecting groups are presented in the final paragraph of page 4 of the specification as filed. Applicants note that the passage at page 4 also explicitly states that the protected compound are those in which "reactive carboxy and amino substituents are protected by selectively removable... moieties." The X and Y substituents recited in the claims are bonded to reactive carboxy and amino groups.

Applicants respectfully traverse this rejection, in part, because the term "protecting group" is clearly defined structurally by example in the specification and is also well understood and extensively utilized by those skilled in the art.

Applicants also traverse this rejection because the Office appears to be rejecting the claims under the written description requirement for a failure to provide a sufficient number of working examples. On that basis alone, Applicants respectfully submit that the rejection is improper.

As a threshold consideration, there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. See MPEP §2163 and *In re Wertheim*, 191 USPQ 90 at page 97 (CCPA 1976): "We are of the opinion that the PTO has the initial burden of presenting evidence or reasons why **persons skilled in the art** would not recognize in the disclosure a description of the invention defined by the claims." (Emphasis added.) Note that the written description analysis is based upon what a person skilled in the art would recognize. On this basis, Applicants note that the claims require the use of protecting groups. The structural and functional aspects of protecting groups are extremely well known. (See Exhibit A, more of which below.) Thus, Applicants also traverse this rejection because the Office has not carried its burden in showing that a person skilled in the art would not recognize the invention recited in the claims upon a close reading of the specification.

Applicants further traverse this rejection because both the case law and MPEP §2163 indicate that the written description requirement for a claimed genus may be satisfied by describing:

(a) A "representative number" of species by actual reduction to practice (as has been done here); and/or

(b) by disclosing "relevant, identifying characteristics," such as by describing structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics.

In short, all that is required to satisfy the written description requirement of §112 is to show, essentially by any descriptive or illustrative means, that the Applicant was in possession of the claimed genus. See MPEP §2163(3)(a) and *The Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, at page 1406 (the *Lilly* case).

Applicants respectfully note that are not required to describe in detail or to exemplify every single species falling within the scope of a generic claim in order to satisfy the written description requirement. See, for example, *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976). In the present application, the specification clearly describes a host of protecting groups by systematic name, *i.e.* by their structure. That is, each of the protecting groups recited by systematic name at page 4 can be reduced to one, unambiguous chemical structure that is understood by all chemists of ordinary skill in the art, worldwide. Moreover, the Examples clearly show how these protecting groups are used. See the Examples of di-substituted carboxylic acids starting at page 30 of the application as filed, which demonstrates the use of protecting groups including methyl, Boc, TBS, and tosyl.

Having presented a large array of protecting groups by way of both an exemplary list, and several working examples, Applicants submit that the written description requirement has been satisfied. Defining a generic term by listing a number of exemplary species that fall within the generic term, as well as working Examples, is a perfectly valid and **approved** approach to defining a generic term. See MPEP §2164.08 and *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971): "How a teaching is set forth, **by specific example** or broad terminology, is not important." (Emphasis added.)

Moreover, what is well-known in the art is best omitted from the specification. MPEP §2164.08 and *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). Protecting groups are

extremely well-known in the scientific literature and extensively used in the claims of issued U.S. patents. When the **claims** of U.S. patents are searched for the exact phrase "protecting group" and the search phrase explicitly **excludes** the traditional Markush introductory phrase "selected from", the USPTO database reveals that 795 patents have been issued since 1976 that contain the unqualified phrase "protecting group" **within the claims**. The exact search query utilized to generate this result was: ACLM/"protecting group" ANDNOT "selected from". The first page of the results from this query is attached hereto and incorporated herein as Exhibit A. Applicants include this list not as a comparison between the present application and applications that came before it, but to demonstrate, by way of objective scientific evidence (namely issued U.S. patents) that the unqualified phrase "protecting group" is well understood in the art, unambiguous in its scope, structural, and extensively utilized in the chemical literature as represented by issued U.S. patents.

Regarding the controlling law with respect to written description, Applicants respectfully take exception to the Office's citation to the *Lilly* case, 43 USPQ2d 1398 (Fed. Cir. 1997) and its selective quotation from the *Fiers v. Revel* case (25 USPQ2d 1601 (Fed. Cir. 1993) as providing the controlling law with respect to the written description requirement of §112, first paragraph. Specifically, the often-cited quotation from *Fiers* is that "disclosure sufficient to satisfy the written description requirement... must include a precise definition of DNA, such as by structure, formula, chemical name, or physical properties" was contained in dictum and **was not** the holding of the Court

As a result, the above quote from *Fiers* **is not** a controlling statement on the written description requirement. (Note also that the string of requirements is in the alternative.) Contrary to Judge Lourie's above-quoted dictum from *Fiers*, it has **never** been the law that an Applicant must know the structure of a compound (DNA, protein, protecting group, or otherwise) in order to satisfy the written description requirement of §112, first paragraph.

The controlling law in this instance is provided by *In re Fisher*, 166 USPQ 18 (CCPA 1970). In *Fisher*, the question was whether the claims of a CIP application (drawn to a protein) were entitled to the filing date of the parent application. In *Fisher*, it was undisputed that the amino acid sequence of the protein claimed in the CIP **was not** disclosed in the parent application,

and further that *Fisher* **did not** know the amino acid sequence at the time the parent application was filed (166 USPQ at 21). The only disclosure in the parent application was a process for extracting the protein from the pituitary glands of certain animals. However, an article which appeared after the filing of the CIP application confirmed that the claimed sequence was, in fact, the sequence of protein described in the parent application. The CCPA **held** that the claimed structure was inherent in the description contained in the parent application, and therefore the parent application described the protein to the level required by §112, first paragraph.

As applied to the present situation, *Fisher* makes clear that the written description requirement of §112 is satisfied by the disclosure of chemical structures (*i.e.*, the list of protecting groups at the bottom of page 4 of the specification as filed) having specific and known properties - in this instance, the ability to act as amino or carboxy protecting groups. The present specification clearly describes (by way of both an exemplary list and a host of working Examples) a number of suitable protecting groups that can be used in the claimed invention. And, as noted above, the law does not mandate that the specification recite every single protecting group which may function in the invention in order to satisfy §112, first paragraph.

In short, the specification clearly shows that Applicants were, at the time of filing, in possession of protecting groups for the X and Y substituents recited in the claims. The specification contains working Examples of how the protecting groups are used. Having done so, it is respectfully submitted that Applicants are entitled to a broader scope of claim coverage than simply the scope of the exemplified species of protecting groups presented in the specification.

The *Lilly* case does not support the Office's position because in the *Lilly* case the plaintiffs **never** described any aspect of the claimed human cDNA beyond the amino acid sequence it was to encode. The only cDNA sequence contained in the disputed specification in *Lilly* was that of a **rat** cDNA analogous to the claimed human cDNA. Having failed to describe **any** characteristics of the claimed **human** cDNA itself (*e.g.*, structure, formula, or physical properties, as noted in *Fiers*), the Court in *Lilly* held that plaintiffs did not adequately describe by way of written description a cell transformed to contain a **human** cDNA.

The *Lilly* case clearly supports Applicants' position because the present specification describes **working examples** of protecting groups that can be used in the claimed compounds and

also includes an **exemplary list** of other protecting groups that can be used. In other words, the present specification contains the missing material that the Court said was required in the *Lilly* case: both a structure **and** a relationship that links that structure to a function - a chemical structure that functions as a protecting group for either a carboxy group or an amino group. The description in the present specification is not merely functional. It's both structural **and** functional. The *Lilly* case, in contrast, stands for the proposition that a definition by function **alone** "does not suffice" to describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." See *Eli Lilly*, 43 USPQ2d at 1406. In stark contrast, the present specification does not describe the protecting groups by function alone, but also includes an extensive list of protecting groups recited by their **structure**, as well as a host of working examples. In particular, see the list at the bottom of page 4 of the specification and the Examples. Having set forth structures for a host of protecting groups and their corresponding functions, Applicants submit that the specification provides an adequate written description of the claimed subject matter.

In short, the present application contains and exemplifies a host of protecting groups, including working examples of how the protecting groups are used in the manufacture of the claimed compounds. The objective scientific literature clearly demonstrates that the phrase "protecting groups" is well understood to those of skill in the art. It is therefore submitted that claiming the compounds using the unqualified phrase "protecting group" is in no way runs afoul of 35 USC §112, first paragraph.

With respect to the *number* of protecting groups disclosed in the specification, Applicants note that the list at the bottom of page 4 recites a rather large number of protecting groups, 28 by Applicants' count. Having described by structure a large number of suitable protecting groups an provided a number of working examples, Applicants respectfully submit that they are entitled to recite in their claims the genus "amino-terminal protecting group," and the genus "carboxy-terminal protecting group."

In support of this contention, Applicants note that there are a number of cases wherein the disclosure of only a single species was sufficient for purposes of the written description requirement to claim an entire genus. See, for example, *In re Herschler*, 200 USPQ 711, 714

(CCPA 1979), wherein the Court held that the disclosure of corticosteroid in DMSO was sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because:

> Use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description.

See also *In re Smythe*, 178 USPQ 279, 285 (CCPA 1973). Here, the phrase "air or other gas which is inert to the liquid" was found to be sufficient to support a claim to "inert fluid media" because the description of the properties and functions of the air or other gas-segmentizing medium would suggest to a person skilled in the art that applicant's invention includes the use of an "inert fluid" broadly.

In the present situation, Applicants have disclosed 28 suitable protecting groups for use in the invention, and have exemplified by way of working examples how to use these protecting groups. Thus, Applicants have disclosed both representative structures, as well as the functionality of the protecting groups. Thus a person of ordinary skill in the art is clearly informed by the specification as filed that other protecting groups beyond those explicitly disclosed in the specification can also be used in the claimed invention.

In light of the above comments and the attached Exhibit A, Applicants respectfully submit that the rejection under §112, first paragraph (written description) is untenable. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1-11 and 14 Under §112, First Paragraph (Enablement):

This rejection is respectfully traversed because one of skill in the art is given ample information in the application as filed to make and use the compounds as broadly as they are claimed.

With regard to the phrase "protecting group," the comments made above with respect to the written description requirement are repeated herein with respect to the enablement requirement (to the extent applicable). Applicants are aware that the enablement requirement of §112, first

paragraph is distinct from the written description requirement, but the two requirements are intertwined. Thus, the remarks made above with respect to protecting groups and the requirements of §112 are incorporated herein by reference.

Specifically addressing the enablement requirement, protecting groups for amino and carboxy functionalities are exceedingly well known, extensively used in the chemical arts, and extensive knowledge of how they are used is clearly attributable to a synthetic organic chemist ordinarily skilled in the field. A patent specification is not aimed at John Q. Public, but, in this instance, the ordinarily skilled synthetic chemist – *i.e.*, a Ph.D.-level chemist. As noted above, the patent literature itself contains a very large number of patents that use the unqualified phrase "protecting group" within their claims.

Moreover, a cursory search of the available literature with respect to protecting groups demonstrates that protecting groups and how to use them are extensively reviewed, cataloged, and compiled in the literature. In other words, the storehouse of knowledge that can be imputed to the ordinarily skilled chemist is very large. In fact, there are a number of well-known text books and monographs whose sole topic is protecting groups. See, for example, "Protecting Groups, 3rd Edition" by Philip J. Kocienski, published by Georg Thieme Verlag, copyright 2005, ISBN 1588903761; "Protecting Group Chemistry," by Jeremy Robertson, published by Oxford University Press, copyright 2000, ISBN 0198502753; "Protecting Groups in Organic Synthesis," by James R. Hanson, published by Sheffield Academic Press, copyright 2000, ISBN 185075957X; "Activating Agents and Protecting Groups, Handbook of Reagents for Organic Synthesis," Anthony J. Pearson and William R. Roush (editors), published by Wiley, copyright 1999, ISBN 0471979279, and "Greene's Protective Groups in Organic Synthesis, 4th Edition" by Peter G. M. Wuts and Theodora W. Greene, published by Wiley-Interscience, copyright 2006, ISBN 0471697540. All of these books remain in print and can be purchased on-line at www.Amazon.com. The Wuts & Green offering, which "continues to be a comprehensive guide to the techniques for the formation and cleavage of protective groups," (*Journal of the American Chemical Society*, vol. 29, no. 4, January 31, 2007), runs more than 1,000 pages.

In short, a chemist of ordinary skill in the art does not need to exercise any undue experimentation to find a suitable protecting group to use in the present invention – he or she can

simply select a group from those listed at the bottom of page 4 of the application as filed. If a different protecting group is desired, one only need to look in the books that are readily available, such as "Green's Protective Groups in Organic Synthesis." This is nothing more than routine experimentation, a huge amount of which is perfectly permissible under the enablement requirement of §112, first paragraph. The key word in the phrase "undue experimentation" is "undue."

There is a distinct difference between effort, even titanic amounts of effort, and "undue" effort. The law in this regard is quite clear: The key concept in undue experimentation is "undue," not "experimentation." See *In re Angstadt*, 190 USPQ 214 (CCPA 1976). In short, satisfaction of the enablement requirement of §112 is not voided by the necessity for experimentation, even huge amounts of experimentation. A considerable amount of experimentation is permissible if it is routine or if the specification provides a reasonable amount of guidance with respect to how the experiments should proceed. See the *Angstadt* case and see also *In re Jackson*, 217 USPQ 804 (Bd. App. 1982).

That last point bears repeating: a considerable amount of experimentation is permissible if it is routine or if the specification provides a reasonable amount of guidance with respect to how the experiments should proceed. On this point, Applicants note that the specification as filed contains a rather extensive teaching of how to fabricate the claimed compounds. Additionally, the claimed compounds include an extremely limited substitution pattern, and all of the variables are attached to the core structure via an exocyclic methylene group.

On this last point, the Office states that "The structures of possible variants for... R^1 [and] R^2 are sufficiently diverse that one... would not be able to predict their structures and/or reactivity in the oligomeric compounds." See the top of page 12 of the Office Action. The first part of this statement is a *non sequitur*. One of skill in the art need not "predict the structures" of the possible variables for R^1 and R^2. The **structures** themselves are unambiguously set forth in the specification as filed. In short, there is nothing at all ambiguous or unclear about the structural recitation set forth at, for example, page 3, line 1, to page 4, line 15 of the specification as filed. The chemical structures for R^1 and R^2 are clearly set forth in the application as filed, so no "prediction" with regard to structure is required. The primary structure of the ultimate

compounds also need not be predicted. The individual monomers are linked together as described in the specification, monomer-by-monomer. So there is no need for any prediction regarding the structure of the claimed compounds.

Regarding reactivity, Applicants note that the claimed compounds are fabricated as monomers, and then the monomers are linked together by a general scheme that will work for any monomer "A" of the type recited in the application. The selection of possible monomers is actually quite limited – the two core structures shown in Claim 1, which bear only two variables, R^1 and R^2. In the great scheme of chemical patent claims, this is a relatively small and well-contained set of Markush groupings. Thus, at page 30, the application sets forth a general scheme for fabricating the protected, di-substituted monomer (*i.e.*, the monomer with the amino and carboxy termini protected from further reaction). Compound 8, for example, at the bottom of page 3, shows a protected, di-substituted monomer wherein one of R^1 or R^2 is hydrogen (thus yielding a methyl group) and the other of R^1 or R^2 is methoxy. The same reaction scheme can be used to fabricate other di-substituted, protected monomers, as noted at the top of page 31 of the specification. These additional working examples at the top of page 31 include alkyloxy and aryl for R^1 and R^2, as well as ^{13}C-labeled versions of the monomer. Other aryl groups will react in an analogous fashion to the aryl shown at the top of page 31. Likewise, sulfur-containing groups will reaction in the same fashion as oxygen-containing groups; oxygen and sulfur are in the same family on the periodic table of elements. And that in every instance, R^1 and R^2 bind to an identical moiety, namely an exocyclic methylene group. Thus, the extent of variability in the reactivity of the R^1 and R^2 substituents is far more narrow than the Office asserts. In short, the reactivity of all of the possibilities for R^1 and R^2 as recited in claim 1 will be roughly the same as the working examples presented in the specification due to the fact that the couplings all take place at the same type of moiety (the exocyclic methylene group), and because the recited substituents react in a fashion analogous to the working examples presented in the application as filed.

The monomers so fabricated are then linked using general reaction schemes that will work for any monomer "A". Two general reaction schemes for coupling the monomers together are presented at page 9, lines 1-25 of the application as filed. Specific working examples of the coupling are presented in the Example starting at page 34, line 10. The coupling reaction itself is

analogous to conventional peptide synthesis. There are only two functionalities at play, the amino terminus and the carboxy terminus of each monomer. Thus, the monomers can be linked quite easily using the coupling chemistry presented in the application as filed in a reiterative fashion to build an oligomer of the desired length and sequence.

Applicants therefore submit that Office has not properly presented a *prima facie* finding of lack of enablement. The Office has the burden of providing sound scientific reasons, supported by the record, *why* the specification fails to properly enable the claims. (See *In re Angstadt*, 190 USPQ 214 (CCPA 1976).) As part of that burden, the Office must present evidence showing that the disclosure requires **undue** experimentation. (*Id.* at 219.) While some routine experimentation may be required to optimize any given coupling reaction, routine experimentation is perfectly acceptable under the enablement requirement of §112, first paragraph.

Applicants therefore submit that the rejection of Claims 1-11 and 14 under §112, first paragraph (enablement) is improper. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1, 2, 4, 5, 10, and 11 for Obviousness-Type Double-Patenting in View of U.S. Patent No. 6,710,186:

This rejection has been overcome by the Terminal Disclaimer and Certification Under §3.73.(b) file herewith. Withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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